

CLAIMS:

1. A purified protein which is:

(1) a protein having the amino acid sequence as shown in SEQ ID NO: 1, or

5 (2) a modified protein of the protein (1) having the amino acid sequence as shown in SEQ ID NO: 1 in which 1 or 2 amino acids are deleted, to which 1 or 2 amino acids are added or in which 1 or 2 amino acids are substituted by other amino acids, the modified protein (2) having a ligand
10 binding activity and a signal transduction activity, each being 0.01 to 100 times that of the protein (1); or

an amide of the protein (1) or (2) having -CONH₂ in place of -COOH at the C-terminal or on a side chain at a position other than the C-terminal or an ester of the
15 protein (1) or (2) having -COOR in place of -COOH at the C-terminal or on a side chain at a position other than the C-terminal in which R is a C₁₋₆ alkyl group, a C₃₋₈ cycloalkyl group, a C₆₋₁₂ aryl group, a C₇₋₁₄ aralkyl group or a pivaloyloxymethyl group; or

20 a protected derivative of the protein (1) or (2) or the amide or ester thereof, in which the amino group of N-terminal methionine residue is protected by a C₁₋₆ acyl group or an -OH, -SH, amino, imidazole, indole or guanidino group on a side chain of an amino acid residue is protected
25 by a C₁₋₆ acyl group; or

a salt of the protein (1) or (2), a salt of the amide or ester, or a salt of the protected derivative.

2. A purified protein which is:

(1) a protein having the amino acid sequence as shown in SEQ ID NO: 5, or

(2) a modified protein of the protein (1) having the amino acid sequence as shown in SEQ ID NO: 5 in which 1 or 2 amino acids are deleted, to which 1 or 2 amino acids are added or in which 1 or 2 amino acids are substituted by other amino acids, the modified protein (2) having a ligand binding activity and a signal transduction activity, each being 0.01 to 100 times that of the protein (1); or

an amide of the protein (1) or (2) having $-\text{CONH}_2$ in place of $-\text{COOH}$ at the C-terminal or on a side chain at a position other than the C-terminal or an ester of the protein (1) or (2) having $-\text{COOR}$ in place of $-\text{COOH}$ at the C-terminal or on a side chain at a position other than the C-terminal in which R is a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, a C_{6-12} aryl group, a C_{7-14} aralkyl group or a pivaloyloxymethyl group; or

a protected derivative of the protein (1) or (2) or the amide or ester thereof, in which the amino group of N-terminal methionine residue is protected by a C_{1-6} acyl group or an $-\text{OH}$, $-\text{SH}$, amino, imidazole, indole or guanidino group on a side chain of an amino acid residue is protected by a C_{1-6} acyl group; or

a salt of the protein (1) or (2), a salt of the amide or ester, or a salt of the protected derivative.

3. The purified protein according to claim 1, which is the protein (1) or a salt thereof.

4. The purified protein according to claim 2, which is the protein (1) or a salt thereof.

5. A partial peptide having at least 20 amino acids of the protein as defined in claim 1 or 2; or

an amide of the partial peptide having $-\text{CONH}_2$ in place of $-\text{COOH}$ at the C-terminal or on a side chain at a position other than the C-terminal or an ester of the partial peptide having $-\text{COOR}$ in place of $-\text{COOH}$ at the C-terminal or on a side chain at a position other than the C-terminal in which R is a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, a C_{6-12} aryl group, a C_{7-14} aralkyl group or a pivaloyloxymethyl group; or

a protected derivative of the partial peptide or the amide or ester thereof, in which the amino group of N-terminal methionine residue is protected by a C_{1-6} acyl group or an $-\text{OH}$, $-\text{SH}$, amino, imidazole, indole or guanidino group on a side chain of an amino acid residue is protected by a C_{1-6} acyl group; or

a salt of the partial peptide, a salt of the amide or ester, or a salt of the protected derivative.

6. The partial peptide according to claim 5, which contains a region which is analyzed to be an extracellular region in a hydrophobic plotting analysis.

7. A polynucleotide having a base sequence encoding the protein (1) or (2) as defined in claim 1.

8. The polynucleotide according to claim 7, which is DNA.

9. The polynucleotide according to claim 7, which contains the base sequences as shown in SEQ ID NO: 2.

10. A polynucleotide having a base sequence encoding the protein (1) or (2) as defined in claim 2.

11. The polynucleotide according to claim 10, which is DNA.

12. The polynucleotide according to claim 10, which contains the base sequences as shown in SEQ ID NO: 6.

5 13. A recombinant vector containing the polynucleotide as defined in any one of claims 7 to 9.

14. The recombinant vector according to claim 13, which is an expression vector comprising a promoter upstream of the polynucleotide.

10 15. The recombinant vector according to claim 14, which is plasmid pAK-rOT7T175.

16. A host cell transformed with the recombinant vector as defined in claim 13, 14 or 15.

15 17. The host cell according to claim 16, which is a CHO cell transduced by plasmid pAK-rOT7T175.

18. A recombinant vector containing the polynucleotide as defined in any one of claims 10 to 12.

19. The recombinant vector according to claim 18, which is an expression vector comprising a promoter upstream
20 of the polynucleotide.

20. The recombinant vector according to claim 19, which is plasmid vector pCR2.1 into which the polynucleotide of claim 9 is introduced.

21. A host cell transformed with the recombinant
25 vector as defined in claim 18, 19 or 20.

22.. A method for manufacturing the protein (1) or (2) as defined in claim 1, which comprises:

culturing a host cell transformed with an expression vector comprising the polynucleotide as defined in any one of claims 7 to 9 and a promoter upstream of the polynucleotide in a culture medium, to produce the protein
5 (1) or (2), and

purifying the produced protein (1) or (2).

23. A method for manufacturing the protein (1) or (2) as defined in claim 2, which comprises:

culturing a host cell transformed with an
10 expression vector comprising the polynucleotide as defined in any one of claims 10 to 12 and a promoter upstream of the polynucleotide in a culture medium, to produce the protein (1) or (2), and

purifying the produced protein (1) or (2).

15 24. A method for determining whether or not a test compound is a ligand to the protein, amide, ester, protected derivative or salt as defined in any one of claims 1 to 4, which method comprises:

contacting the test compound with the protein,
20 amide, ester, protected derivative or salt; and

determining whether the test compound binds to the protein, amide, ester, protected derivative or salt or provides a cell stimulating activity,

wherein when the test compound binds or provides
25 the cell stimulating activity, the test compound is the ligand.

25. The method according to claim 24, wherein:

the test compound is contacted with a cell transformed with an expression vector containing a polynucleotide having a base sequence encoding the protein (1) or (2) as defined in claim 1 or 2 and a promoter upstream of the polynucleotide; and

the cell stimulating activity is determined.

26. The method according to claim 25, wherein an intracellular Ca^{2+} ion release is determined as the cell stimulating activity.

10 27. The method according to claim 24, wherein:

the test compound is labeled;

the labeled test compound is brought into contact (1) with the protein, amide, ester, protected derivative or salt, (2) with a cell or a membrane fraction thereof where the cell contains the protein or (3) with the protein expressed on a cell membrane of a cell which is transformed with the expression vector as defined in claim 14 or 17; and

whether or not the test compound binds to the protein, amide, ester, protected derivative or salt is determined.

28. A peptide or an amide, ester or salt thereof, which, when in the peptide form, is composed of 8 to 54 amino acid residues including an 8 amino acids sequence from Trp at position 47 to Phe at position 54 of the amino acid sequence as shown in SEQ ID NO: 10.

29. The peptide, amide, ester or salt according to claim 28, which has 8 to 15 amino acid residues.

30. The peptide, amide, ester or salt according to claim 28 or 29, which is the amide having -CONH₂ in place of -COOH at the C-terminal.

31. The amide according to claim 30, which has the amino acid sequence as shown in SEQ ID NO: 10.

32. The amide according to claim 30, which has the amino acid sequence as shown in SEQ ID NO: 11.

33. The amide according to claim 30, which has the amino acid sequence as shown in SEQ ID NO: 12.

34. The amide according to claim 30, which has the amino acid sequence as shown in SEQ ID NO: 13.

35. The amide according to claim 30, which has the amino acid sequence as shown in SEQ ID NO: 14.

36. A pharmaceutical composition comprising:

(a) the peptide, amide or ester as defined in any one of claims 28 to 35 or a pharmaceutically acceptable salt thereof, and

(b) a pharmaceutically acceptable carrier.

37. The pharmaceutical composition according to claim 36, which is a prophylactic or therapeutic drug for a cancer.

38. A method for screening a test compound that alters a binding property between the protein or salt as defined in any one of claims 1 to 4 and a ligand thereof, which method comprises:

(a) bringing the protein or salt in contact with the ligand and the test compound;

(b) determining the amount of the ligand bound to the protein or salt or a cell-stimulating activity of the test compound; and

(c) comparing the amount of the ligand bound to the protein or salt or the cell stimulating activity with a corresponding amount or activity obtained by conducting the steps (a) and (b) without the test compound.

39. The method according to claim 38, wherein the ligand is the peptide, amide, ester or salt as defined in any one of claims 28 to 35.

40. The method according to claim 38 or 39, wherein the ligand used in step (a) is labeled and the amount of the ligand bound to the protein or salt is determined in step (b).

41. The method according to any one of claims 38 to 40, wherein the protein or salt in step (a) is contained in a cell or cell fraction.

42. A kit for screening a compound that alters a binding property between the protein or salt as defined in any one of claims 1 to 4 and a ligand thereof, which comprises:

the protein or salt or a host cell which is transformed with the expression vector as defined in claim 14 or 17; and

the ligand that is labeled.

43. The kit according to claim 42, wherein the ligand is the peptide, amide, ester or salt as defined in any one of claims 28 to 35.

44. The kit according to claim 42 or 43, which further comprises a buffer for assay and washing.

45. An antibody to the protein, amide, ester, protected derivative or salt as defined in claim 1, 2, 3 or 4 or the partial peptide as defined in claim 5 or 6.

46. The antibody according to claim 45, which is a neutralizing antibody to inactivate signal transduction of the protein.

47. A diagnostic composition, which comprises:

10 the antibody as defined in claim 21 or 22, and
a suitable diluent.

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